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Single amino acid substitutions in influenza haemagglutinin change receptor binding specificity.

Rogers GN, Paulson JC, Daniels RS, Skehel JJ, Wilson IA, Wiley DC.

The haemagglutinin (HA) glycoproteins of influenza virus membranes are responsible for binding viruses to cells by interacting with membrane receptor molecules which contain sialic acid (for review see ref. 1). This interaction is known to vary in detailed specificity for different influenza viruses (see, for example, refs 2-4) and we have attempted to identify the sialic acid binding site of the haemagglutinin by comparing the amino acid sequences of haemagglutinins with different binding specificities. We present here evidence that haemagglutinins which differ in recognizing either NeuAc alpha 2 leads to 3Gal- or NeuAc alpha 2 leads to 6Gal-linkages in glycoproteins also differ at amino acid 226 of HA1. This residue is located in a pocket on the distal tip of the molecule, an area previously proposed from considerations of the three-dimensional structure of the haemagglutinin to be involved in receptor binding.

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